



**PARAMETRI DOSIMETRICI
ASSOCIATI A RADIONECROSI
(RN) DOPO RE-IRRADIAZIONE
CON RADIOCHIRURGIA (SRS) DI
METASTASI CEREBRALI**

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SINGLE DOSE RADIOSURGICAL TREATMENT OF RECURRENT
PREVIOUSLY IRRADIATED PRIMARY BRAIN TUMORS AND BRAIN
METASTASES: FINAL REPORT OF RTOG PROTOCOL 90-05

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The maximum tolerated doses of reirradiation

doses	diameter
24 Gy	∅ < 20 mm
18 Gy	∅ 21-30 mm
15 Gy	∅ 31-40 mm

IRRADIATED VOLUME AS A PREDICTOR OF BRAIN RADONECROSIS AFTER LINEAR ACCELERATOR STEREOTACTIC RADIOSURGERY

Int. J. Radiation Oncology Biol. Phys., Vol. 77, No. 4, pp. 996–1001, 2010

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2010

63 pts-173 lesions

SRS mean dose 18 Gy

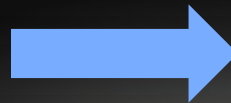
63 % (109 lesions) WBRT+ SRS

Diagnosis with MR imaging (RN 14%, 24/173)

Multivariate analysis: V8 Gy-V16 Gy most
predictive of symptomatic RN ($p < 0.0001$)

V10 Gy > 10.5 cm³

V12 Gy > 7.9 cm³



Significant rise of RN rates (75°-90° percentiles)

(11%-35%)

Significance of target location relative to the depth from the brain surface and high-dose irradiated volume in the development of brain radionecrosis after micromultileaf collimator-based stereotactic radiosurgery for brain metastases

Kazuhiro Ohtakara · Shinya Hayashi ·
Noriyuki Nakayama · Naoyuki Ohe ·
Hirohito Yano · Toru Iwama · Hiroaki Hoshi

2012

J Neurooncol (2012) 108:201–209

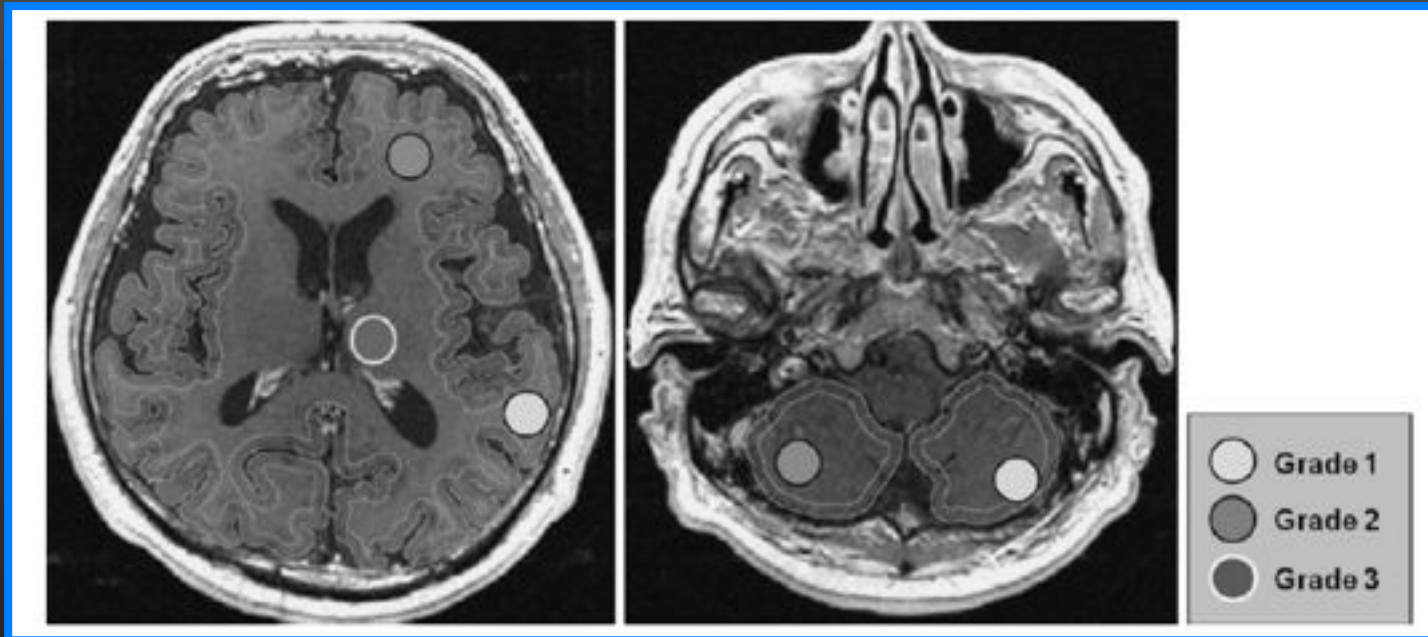
**57 pts 131 lesions SRS (24 pts 57 lesions WBRT+SRS)
Symptomatic -asymptomatic RN**

Diagnosis with MR imaging (RN 15%, 20/131)

Low-dose irradiated isodose volume V10 Gy, V12 Gy

High-dose irradiated isodose volume V15 Gy, V22 Gy

LESIONS LOCATION



LOCATION GRADE

GRADE		LOCATION
1	SUPERFICIAL	≤ 5 mm from the brain surface
2	DEEP	> 5 mm from the brain surface (white matter)
3	CENTRAL	Brainstem, cerebellar peduncle, thalamus, hypothalamus, basal ganglion

Table 4 Multivariate analysis of factors for predicting S-RN and all RN (S-RN + A-RN)

		-2 log likelihood	Chi squared	P value	Variables	Partial regression coefficient	P value	Adjusted HR (95% CI)
Total	S-RN	66.68	38.63	<0.001	Location grade	2.14	<0.001	8.516 (3.14–23.09)
					V12 Gy	0.20	<0.001	1.224 (1.10–1.36)
					RPA class	-1.41	0.016	0.243 (0.08–0.77)
	All RN	128.98	48.73	<0.001	Location grade	1.60	<0.001	4.943 (2.32–10.55)
					V12 Gy	0.12	0.001	1.131 (1.05–1.22)
					V22 Gy	0.37	0.006	1.447 (1.12–1.88)
Non-WBRT	S-RN	28.94	24.50	<0.001	V22 Gy	1.18	0.001	3.241 (1.62–6.50)
					Sawaya's functional grading	1.71	0.011	5.525 (1.49–20.50)
	All RN	56.45	42.10	<0.001	V22 Gy	0.85	<0.001	2.348 (1.65–3.34)
					Location grade	1.70	0.002	5.483 (1.92–15.70)
WBRT	S-RN	15.71	26.25	<0.001	Location grade	2.25	0.009	9.529 (1.74–52.14)
					V15 Gy	0.50	0.013	1.644 (1.11–2.44)
	All RN	28.24	33.91	<0.001	V15 Gy	0.56	<0.001	1.750 (1.30–2.37)
					Location grade	1.65	0.012	5.205 (1.43–18.91)

Univariate analysis: CTV , max diameter, location grade, Sowaya's grading, V8-V24 tot pts.

Table 5 Receiver operating characteristic (ROC) curve analysis of the irradiated isodose volumes for predicting the development of S-RN and all RN

			AUC (95% CI)	<i>P</i> value ^a	Cutoff value (cm ³)	Sensitivity	Specificity	OR
Total	S-RN	V12 Gy	0.84 (0.77–0.92)	<0.001	8.39	0.91	0.77	32.86
		V22 Gy	0.65 (0.43–0.88)	0.095	1.82	0.64	0.83	8.75
	All RN	V12 Gy	0.83 (0.74–0.91)	<0.001	8.39	0.85	0.81	24.29
		V22 Gy	0.69 (0.53–0.85)	0.007	1.82	0.60	0.86	9.60
Non-WBRT	S-RN	V12 Gy	0.84 (0.74–0.93)	0.006	8.87	0.83	0.76	16.25
		V22 Gy	0.92 (0.86–0.99)	0.001	2.62	0.83	0.91	51.67
	All RN	V12 Gy	0.75 (0.61–0.90)	0.008	8.62	0.82	0.79	17.31
		V22 Gy	0.84 (0.69–0.99)	<0.001	2.14	0.82	0.84	23.85
WBRT	S-RN	V12 Gy	0.86 (0.75–0.97)	0.009	8.39	0.80	0.81	16.80
		V15 Gy	0.88 (0.78–0.97)	0.006	5.61	0.80	0.85	22.00
		V18 Gy	0.73 (0.42–1.00)	0.088	1.72	0.80	0.81	16.80
	All RN	V12 Gy	0.91 (0.84–0.99)	<0.001	8.39	0.89	0.87	56.00
		V15 Gy	0.93 (0.86–0.99)	<0.001	5.20	0.89	0.90	68.80
		V18 Gy	0.70 (0.46–0.93)	0.063	1.72	0.67	0.83	10.00

OUR EXPERIENCE

2001-2008

69 pts with cerebral metastasis

WBRT 10x3Gy/5x4Gy ⇒ reirradiation SRS (PD)

Radionecrosis diagnosed by MR & SPECT- mibi



4/69 (6%)
RADIONECROSIS

Data upgrading

6/69 (8%)
RADIONECROSIS

PATIENTS CHARACTERISTICS

MALE/FEMALE	3/3
median AGE	59 yy
KPS	90%
Median RPA class	2
HYSTOLOGY	NSCLC 3 (50%) BREAST adenocarcinoma 2 (33%) COLON adenocarcinoma 1 (17%)

All pts with STABLE SYSTEMIC DISEASE

All pts were ASYMPTOMATIC

TREATMENT CHARACTERISTICS

Median INTERVAL TO REIRRADIATION	17 months (range, 4-29)
Median TARGET VOLUME	4,2 cm ³ (range, 0,1-18,6)
Median SRS DOSE	19 Gy (range, 16-21)
Median FOLLOW-UP	13 months (range, 11-36)

RESULTS

PATIENTS	DOSE	lesion size cm ³	V10>10,5c m ³	V12>7,9 cm ³	V15>5,20c m ³	V22>2,14c m ³
1	20	12	39,75	31,47	22	0
2	16	0,3	8,36	5,99	2,72	0,00
3	17	18,6	53,4	44,16	32,16	0
4	23	1,6	11,16	8,11	5,54	1,44
5	25	0,1	3,26	2,31	1,43	0,33
6	18	6,8	26,9	21,1	14,7	0

RESULTS

PATIENTS	DOSE	lesion size cm ³	V10>10,5c m ³	V12>7,9 cm ³	V15>5,20c m ³	V22>2,14c m ³
1	20	12	39,75	31,47	22	0
2	16	0,3	8,36	5,99	2,72	0,00
3	17	18,6	53,4	44,16	32,16	0
4	23	1,6	11,16	8,11	5,54	1,44
5	25	0,1	3,26	2,31	1,43	0,33
6	18	6,8	26,9	21,1	14,7	0

4/6 PTS (67%) HIGHER IRRADIATION VOLUMES

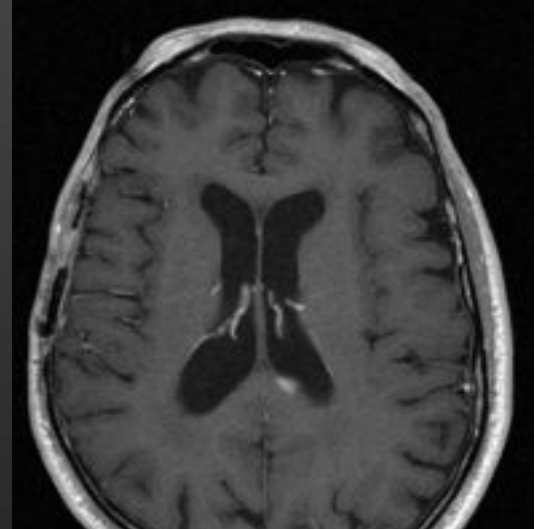
LOCATION GRADE



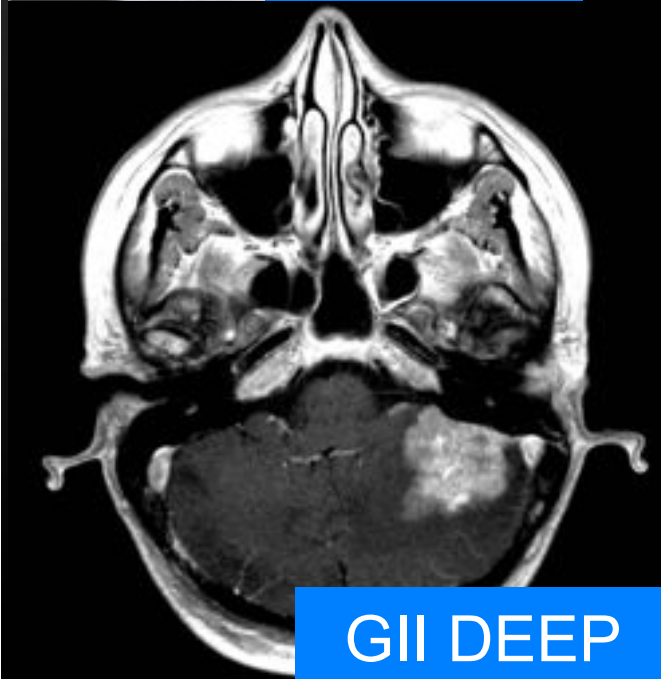
GII DEEP



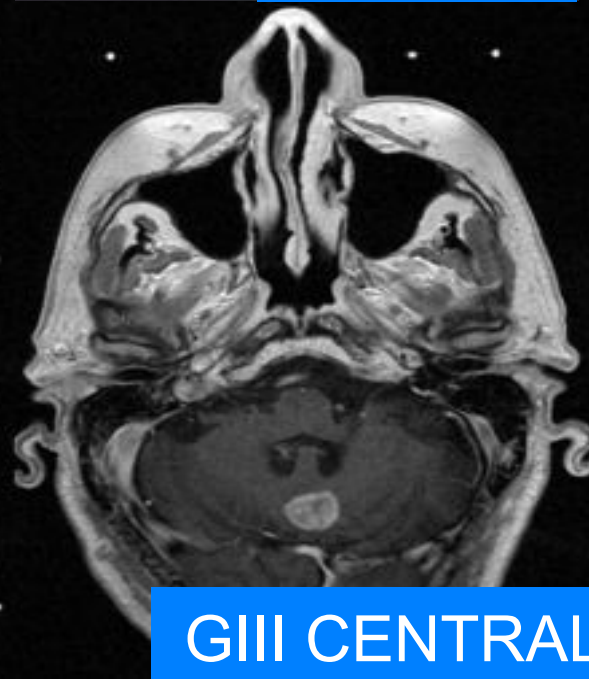
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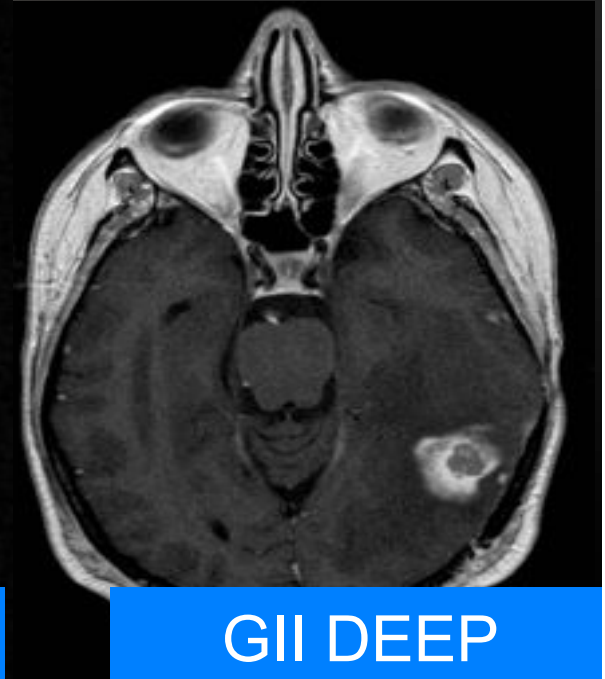
GIII CENTRAL



GII DEEP



GIII CENTRAL



GII DEEP

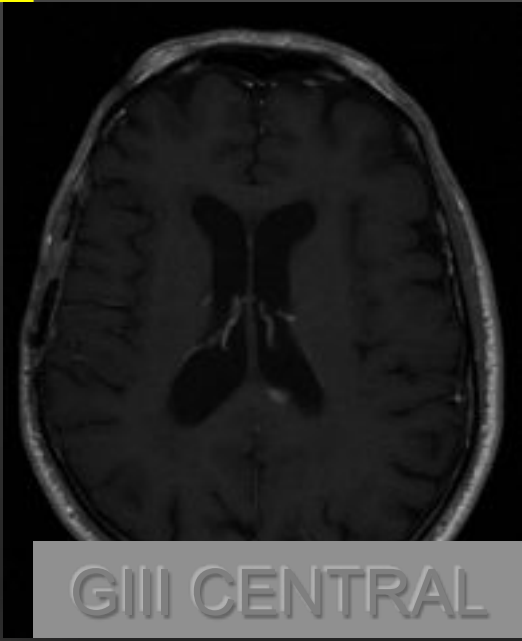
LOCATION GRADE



GII DEEP



GII DEEP



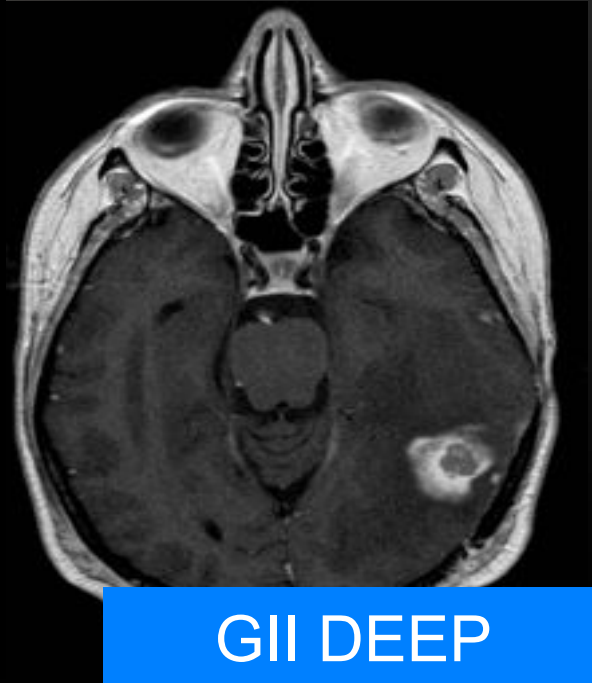
GIII CENTRAL



GII DEEP



GIII CENTRAL



GII DEEP

CONCLUSIONS

- 1. In our experience, radionecroses are related to higher Vs (i.e., V10Gy, V12Gy, V15Gy)**
- 2. Both lesion diameters suggested by RTOG trial and Vs influence incidence of radionecroses**
- 3. Also location lesion can influence the risk of radionecroses**
- 4. For lesions with high risk of radionecroses is preferable fractionated stereotactic radiotherapy**

Thank you

